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Date: December 7, 2004

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C/M No: 081476-0305616

Comments:

Applicants: Melmed *et al.*

Serial No.: 09/978,146

Filing Date: October 15, 2001

For: *PTTG KNOCKOUT RODENT AS A MODEL TO STUDY  
MECHANISMS FOR VARIOUS PHYSIOLOGICAL PHENOMENA,  
INCLUDING DIABETES*

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PATENT  
81476-305616

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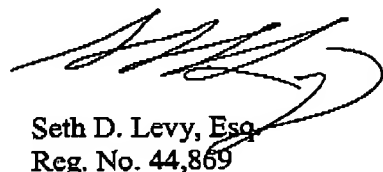
Dear Examiner Chen:

Thank you for speaking with me about revisions to the claims of this application. In our telephone conversation, you indicated that claims 42-54 and 56-59 were in condition for allowance (claims 1-51 and 55 were previously canceled), but that claims 60-65 may not be allowable under 35 U.S.C. § 101, for a lack of utility.

The Applicants hereby request the cancellation of claims 60-65 via Examiner's Amendment. In addition, also via Examiner's Amendment, please add new claim No. 66, which is listed on the attached page and, per your suggestion, describes a method for screening drug candidates for treating certain disease conditions using the null mutant mouse of the invention.

Please let me know if this new claim is acceptable. If you have any questions or concerns, please do not hesitate to contact me directly. Thank you for your continued assistance in this matter.

Best regards,



Seth D. Levy, Esq.  
Reg. No. 44,869

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**APPLICANTS' PROPOSED NEW CLAIM**

66. (New) A method for screening a drug candidate for therapeutic treatment of a disease condition selected from the group consisting of diabetes, hyperglycemia, hypoinsulinaemia, and hypoleptinemia, comprising:
- providing a null mutant mouse comprising in its germ cells an artificially induced PTTG null mutation on both PTTG alleles, wherein said mutation results in said mouse exhibiting at least one phenotype selected from the group consisting of hyperglycemia, hypoinsulinaemia, hypoleptinemia, diabetes, chromosomal aneuploidy, premature centromere division, chromosomal damage, aberrant mitotic cellular division, thrombocytopenia, thymic hyperplasia, splenic hypoplasia, testicular hypoplasia, and female subfertility, the prevalence of which is greater than in a mouse lacking said mutation;
  - administering said drug candidate to said mouse; and
  - determining potential efficacy of said drug candidate for the treatment of said disease condition based on a response of said mouse to said drug candidate.